

## LETTERS TO THE EDITOR

Larval Therapy for a Leg Ulcer with Methicillin-resistant *Staphylococcus aureus*

Sir,

Antibiotic resistance of bacteria is a growing problem. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a frequent nosocomial pathogen in many countries, with a high incidence in southern Europe, but with a lower incidence in Scandinavia (1). MRSA is most commonly isolated from ulcers and the respiratory tract (1). We report here a case of a leg ulcer carrying MRSA, which was treated with the larvae of the blow-fly *Lucilia Sericata*.

## CASE REPORT

An 82-year-old man presented with a history of recurrent leg ulcers since the early 1970s. He was a heavy smoker with hypertension, chronic atrial fibrillation, congestive heart failure and arterial insufficiency in his legs. His medical history also included protein-S deficiency and he had had several episodes of deep venous thrombosis and a pulmonary embolus. His varicose veins were operated on in the early 1980s. His venous status had not been further investigated. A new ulcer had formed on the right leg just above the lateral malleolus in January 1995. One month later, several palpable purpuric lesions developed in the skin and a vasculitic disorder was verified histologically. The patient was admitted for hospital care and treated with oral steroids. The signs of vasculitis faded with the therapy. The cause of the vasculitis was never disclosed. The ulcer progressed even when all signs of vasculitis had subsided and the patient became increasingly immobile. The systolic toe pressure in his right foot was 46 mmHg in April 1995 and the ankle/brachial pressure index was 0.56. Angiographic examination showed several stenotic changes. The ulcer was thought to be caused by a combination of venous and arterial insufficiency. Colour-duplex ultrasound analysis of his arterial circulation in 1997 showed that the patient had critical ischaemia suitable for arterial reconstruction. The ulcer pain was disabling and could not be sufficiently reduced with a combination of paracetamol and morphine. Dizziness and poor eyesight also restricted his mobility. In November 1995 the patient moved to a nursing home. In June 1997 MRSA was found in his ulcer for the first time, which made a vascular operation impossible. The patient was isolated in his room at the nursing home to avoid spread of the MRSA (2). His ulcer was dressed three times weekly with a cadexomer iodine dressing (Iodosorb®, Smith & Nephew, Med Ltd,

UK). He was also treated with a short-stretch bandage (Comprilan®, Beiersdorf AG, Germany), there was no evident oedema. The ulcer progressed despite the treatment, without any signs of healing. He has not received any antibiotic treatment for the MRSA.

In September 1997, the patient was introduced to larval therapy. The total size of the ulcer was 470 cm<sup>2</sup> (Fig. 1). A ring of hydrocolloid dressing (Duoderm®, ConvaTec Ltd, UK) was applied to the intact skin around the ulcer edges (Fig. 2) to protect the skin surrounding the ulcer from the potent proteolytic enzymes in the larval secretions and to minimize the tickling sensation of the larval movements. About 200 larvae, 1–2 mm long were placed in the ulcer (Fig. 2). The ulcer was then covered with a net to avoid larval escape. A top dressing of gauze soaked in saline was placed over the net and held in place with dry gauze. The top dressing was changed after 24 h to a dry gauze dressing and this was changed every 24 h for 3 days, after which the fully grown larvae were removed. The yellowish-green necrosis in the ulcer was removed by the larvae and healthy pinkish granulation tissue could be seen. Larvae are usually flushed down the drain, but since these larvae could hold MRSA, they were dealt with as contagious material.

The ulcer treatment was continued with cadexomer iodine and a short-stretch bandage three times a week, and now the ulcer started to heal. The patient, who initially had been sceptical about the therapy, was now enthusiastic as the ulcer showed improvement.

Another larval application was administered in November 1997. For 3 days the larvae remained in the ulcer without any discomfort to the patient. Two days after removal of the larvae a swab from the ulcer showed that the MRSA had lost its specific resistance-gene due to mutation.

The patient then received a third and final larval treatment shortly after the second one. This time, however, the patient experienced pain after 2 days of therapy and the larvae were removed. Some of them were fully grown and some were small, indicating that there had been little to feed on in the ulcer. The ulcer appeared to be well debrided. The ulcer was then treated as before, with cadexomer iodine and short-stretch compression bandages. Further swabs did not show any signs of MRSA but only of common *S. aureus*. The ulcer size continued to decrease to 8 cm<sup>2</sup> in August 1998 and proceeded to complete healing in November 1998 (Figs 1 and 3). The pain decreased considerably, now sufficiently being controlled by analgesics. The patient was offered vascular reconstructive surgery as he no longer carried MRSA, but he turned the offer down as the pain was bearable.



Fig. 1. The leg ulcer with MRSA in September 1997 before treatment with larvae.



Fig. 2. The ulcer with larvae and a hydrocolloid dressing around the ulcer edges to protect the skin from larval secretions.



Fig. 3. The granulating healing ulcer in August 1998 without MRSA.

## DISCUSSION

Many ulcers have a multifactorial origin, which makes them difficult to treat. We believe that larvae of the blowfly have a place in modern management of difficult-to-treat ulcers. *Lucilia sericata* is the most common larval species used, since they feed on necrotic tissue and leave viable tissue alone. Larval therapy is useful in patients with foul-smelling necrotic ulcers such as gangrene (leg and foot ulcers and decubitus ulcers) needing efficient rapid debridement but has also been suggested to speed ulcer healing (3–7). During the 1930s and 1940s, before the antibiotic era, larval therapy was commonly employed by surgeons in the USA and Europe when treating deep bone or soft-tissue infections (4, 8). However, since the advent of antibiotics larval therapy has been little used. Today most physicians in developed countries are unaccustomed to untreatable bacterial diseases (9). Evolution of bacterial strains resistant to antibiotics is a growing problem and we might need to look for alternative treatments to antibiotics. *S. aureus* is the most common bacterial strain found in leg ulcers (10).

The treatment of choice for MRSA infections is a glucopeptide antibiotic, i.e. teicoplanin or vancomycin (1). This treatment is, however, used only when there are obvious signs of an infection. If MRSA without signs of infection is found, antibiotics should be avoided altogether.

In this case we cannot say with certainty whether the MRSA would have mutated spontaneously without larval therapy. The larvae did, however, induce a healing process in an ulcer of multifactorial origin and reduced the pain of the ulcer. In all probability, the larvae also reduced the amount of bacteria.

There are several mechanisms affecting bacteria, which grow on necrotic tissue. They are destroyed along with the dead tissue in the alimentary tract of the larvae as the larvae feed on the necrotic tissue. The bacteria are also washed out of the ulcer as a result of the increased wound exudate caused by the irritant effect of the larvae and the enzymatic liquefaction of necrotic tissue. Antibacterial agents are present in the larval secretions (7). The antibacterial agents produced by the larvae are of interest, but have not yet been fully investigated. One of the interesting agents is allantoin, which is produced by the lar-

vae and decreases bacterial counts, even though synthetically prepared allantoin has not been proved to have any direct bactericidal properties in ulcers (11). Many studies are more than 50 years old, but newer investigations of the properties of larval secretions have been performed (12).

This is the first case reported in which larval therapy is thought to have played an essential part in the alteration of MRSA into common *S. aureus* as well as having an important impact on the healing of the ulcer. The time of beneficial effect on both MRSA and the ulcer healing coincided with the larval application, supporting our belief that the larvae and no other factor was of importance.

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